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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,205	07/18/2003	Maria Palasis	BSX:233US	2843

32425 7590 11/29/2007

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AFREMOVA, VERA

ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/623,205	PALASIS, MARIA	
	Examiner	Art Unit	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/14/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9-14,17,18,20,21,24-31,35 and 39-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,9-14,17,18,20,21,24-31,35 and 39-49* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/14/2007 has been entered.

Claims 1, 9-14, 17, 18, 20, 21, 24-31, 35, 39-47 as amended and new claims 48 and 49 (9/14/2007) are pending and under examination.

Claim Rejections - 35 USC § 112

Indefinite

Claims 1, 9-14, 17, 18, 20, 21, 24-31, 35, 39-47 as amended and new claims 48 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 14 and 31 are indefinite with regard to the final result or effect of the claimed method. The preambles of these claims recite the intended effect that is formation of muscle cells in the damaged tissues. However, the final active step of the claimed method leads to implantation of the stem cells into the tissue "comprising muscle cells" but not to the production of muscle cells. Thus, the claims are given broadest reasonable interpretation as drawn to implantation of the stem cells into the tissue that comprises muscle cells particularly in view that production of muscle cells immediately from the isolated and implanted stem cells is not disclosed in the as-field specification.

Claims 25 and 40 recites the limitation "GM-CSF", "IL-3" and "SCF" as those engraftment factors that are administered to the patient in the method of claims 14 and 31. There is insufficient antecedent basis for these limitations in the pending claims 14 and 31 wherein these factors were omitted by way of several claim amendments.

Claims 46 and 47 are indefinite because it is unclear when in the method of claim 1 the stem cells "are further defined as hematopoietic stem cells" (claim 46) and when they "are mesenchymal stem cells" (claim 47). It is unclear whether the limitations of claims 46 and 47 refer to a) step of mobilization or to b) step of isolating or to c) step of implantation and/or engraftment. It is unclear what stem cells are isolated and what stem cells are implanted in the method of claims 46 and 47 as it would be intended for "producing a graft of muscle cells". The mixed stem cell populations appear to be intended by applicants in the light of generic disclosure of specification (par. 0025) and it is not particularly clear what cells, when and in what step of the claimed method these stem cells would useful in the presently claimed invention for producing a graft of muscle cells as disclosed. Example 1 describes the use of CD34+ hematopoietic cells, the example 2 is generic with regard to the stem cells and the example 3 does not recite any stem cells. Moreover, no muscle cells formation is disclosed in the as-filed specification in order to clearly define the intended effects recited in the claims.

New matter

Claims 46 and 47 as amended are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Insertion of the limitations drawn to the use of engraftment factors (claim 1, step c) and deletion of some mobilization factors (claim 1, step b) in the method of producing a graft of muscle cells from hematopoietic stem cells (claim 46) or from mesenchymal stem cells (claim 47) have modified the scope of the claims 46 and 47 to the extend that the instant claims 46 and 47 have no support in the as-filed specification.

The insertions of new limitations is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genera that would show possession of the concept of the use of presently claimed mobilization factors and the use of the presently claimed engraftment factors for producing a graft of muscle cells from either hematopoietic stem cells (claim 46) or from mesenchymal stem cells (claim 47).

The generic disclosure provides a generic list of mobilization factors and engraftment factors with regard to mobilization and engraftment of generic cells or generic stem cells (pages 3-4). Accordingly to the applicants' definitions the generic cells or generic stem cells comprises a variety of cells of various lineages and various degree of differentiation commitment (pages 9-10). The as-field specification does not distinguish between mobilization factors and engraftment factors as related to either hematopoietic stem cells (claim 46) or to mesenchymal stem cells. The as-field specification does not distinguish between mobilization factors and engraftment factors as related to producing muscle cells from either hematopoietic stem cells (claim 46) or to mesenchymal stem cells.

The exemplified disclosure does not describe producing muscle cells. The exemplified disclosure does not describe producing a graft with muscle cells obtained from either hematopoietic stem cells (claim 46) or to mesenchymal stem cells (claim 47). There exemplified disclosure does not describe the use of mobilization factors and engraftment factors with regard to mobilization and engraftment of either hematopoietic stem cells (claim 46) or to mesenchymal stem cells (claim 47). Example 1 describes the use of CD34+ hematopoietic cells in the absence of mobilization factors and engraftment factors. Example 2 describes the use of generic stem cells in the absence of mobilization factors and engraftment factors. Example 3 describes the sole use of one mobilization factor G-CSF without any engraftment factors but it remains totally silent with regard to the cells that are collected and that are delivered to myocardium. It is not even clear from the example 3 whether or not the cells are stem cells.

This is not sufficient support for the new genera of mobilization factors and engraftment factors with regard to mobilization and engraftment of either hematopoietic stem cells (claim 46) or to mesenchymal stem cells (claim 47).

This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of limitations drawn to the use of engraftment factors (claim 1, step c) and deletion of some mobilization factors (G-CSF, for example, in claim 1, step b) in the method of producing a graft of muscle cells from hematopoietic stem cells (claim 46) or from mesenchymal stem cells (claim 47) is considered to be the insertion of new matter for the above reasons.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1, 9-14, 17, 18, 20, 21, 24-31, 35, 39-46 as amended and new claims 48 and 49 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Kocher et al. ("Neovascularization of ischemic myocardium by human bone-marrow-derived angioblasts prevents cardiomycete apoptosis, reduces remodeling and improves cardiac function". Nature Medicine. April 2001. Vol. 7, No. 4, pages 430-436) and Kalka et al. ("Transplantation of *ex vivo* expanded endothelial progenitor cells for therapeutic neovascularization". PNAS. March 28, 2000. Vol. 97, No. 7, pages 3422-3427) taken with US 5,199,942 (Gillis), US 7,097,833 (Freyman) and US 6,713, 052 (White et al.).

Claims are directed to a method of producing a graft of muscle tissue in damaged or diseased tissue of a human in need thereof, comprising steps of a) administering a mobilization factor to a donor to mobilize stem cells into peripheral blood, the donor being HLA-matched to a recipient; b) isolating stem cells from peripheral blood of the donor by apheresis; and c) implanting a population of the isolated stem cells into the tissue of recipient in combination with administration of a engraftment factor either concurrently or following the stem cell implantation; whereby implantation produces a graft of muscle tissue in the damaged or diseased tissue. Some claims are/are further drawn to the damaged or diseased tissue(s) including tissue striated muscle, ischemic tissue, necrotic tissue, myocardium, skeletal muscle, heart. Some

claims are further drawn to fractionating the stem cells prior implantation including FACS and density gradient centrifugation. Some claims are further drawn to additional step of ex vivo expanding the cells prior to the implanting step. Some claims are further drawn to implanting the cells at the site of disease or damage. Some claims are further drawn to the use of hematopoietic stem cells in the method for of treating damaged muscle tissue.

The references by Kocher et al. and Kalka et al. are relied for the disclosure of a method of treating damaged or diseased tissue and/or of producing an improved and functional graft of muscle tissue in the damaged or diseased tissue of a mammalian subject by implanting peripheral blood derived stem cells. The cited references teach that transplantation of the donor peripheral blood derived stem cells results in neovascularization and amelioration of the damaged muscle tissues such as striated muscle, ischemic tissue, necrotic tissue, myocardium, skeletal muscle, heart. Both cited references demonstrate that the donor peripheral blood derived stem cells were incorporated or implanted into recipient damaged tissues, thereby, producing an improved and functional tissue "comprising muscle cells" within the broadest meaning of the instant claims. Both cited references recognize the presence of stem cells in circulating blood or peripheral blood and both cited references recognize the peripheral blood as a source of isolation of the stem cells. The reference Kocher et al. also teaches administration of mobilization factors to the donor of the stem cells in order to mobilize the stem cells from bone marrow into peripheral blood of the donor (page 430, col. 2, last par.). The reference Kalka et al. also teaches that *ex vivo* culture strategy allows expansion and considerable increase in the original number of harvested cells (page 3426, col. 2, par. 2). Both cited references suggest that transplantation of stem and/or progenitor cell population has potential to significantly improve damaged or

diseased tissue in patients, and, thus, humans. Both cited references suggest transplantation of stem cells alone or in combination with currently used therapies or with cytokines. For example: see Kocher et al. at abstract and see Kalka et al. at last lines of the articles on page 3427. In particular, the cited reference references by Kocher et al. and Kalka et al. disclose the use of hematopoietic stem cells including CD34+ in the methods for of treating damaged muscle tissue and/or improving cardiac function.

Thus, the general concept and the sequence of active step as disclosed by Kocher et al. and Kalka et al. is the same as encompassed by the presently claimed method comprising stem cell mobilization (recruitment into peripheral blood), stem cell isolation and stem cell implantation or engraftment into damaged muscle tissue for improving biological function of the tissue comprising muscle cells.

The cited references by Kocher et al. and Kalka et al. recognize and suggest combined therapies or transplantation of stem cells with additional drugs but they are lacking particular disclosure about some particular mobilization and engraftment factors.

However, US 5,199,942 (Gillis) teaches administration of mobilization (recruitment) factors prior to harvest of stem cells from peripheral blood and administration of engraftment factors subsequent to implantation of the stem cells (col. 3, lines 29-45) including GM-CSF, IL-3, SCF, IL-1 and others (col. 4, 10-19). US 5,199,942 also teaches *ex vivo* expansion of progenitor cells (col. 3, lines 46-52) in the method for improving cell transplantation. Thus, the general concept and the sequence of active step as disclosed by US 5,199,942 (Gillis) is also the same as encompassed by the presently claimed method comprising stem cell mobilization

(recruitment into peripheral blood), stem cell isolation and stem cell implantation in combination with engraftment factors.

In addition, US 6,713,052 is relied upon for the teaching of Flt-3 as a mobilization factor similar to G-CSF and GM-CSF. US 7,097,833 is relied upon for the teaching about HLA-matching of stem cell donor and recipient in the method of improving function of damaged muscle or heart and also for the teaching about modes of stem cell administration including retrograde perfusion (entire document including col. 3, lines 65-67; col. 6, lines 8-20; col. 10, lines 55-63). The general concept and active step sequence as disclosed by the cited patent US 7,097,833 is the same as encompassed by the presently claimed method comprising mobilization, isolation and implantation of stem cells.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to administer various mobilization and/or engraftment factors in combination with the stem and/or progenitor cell transplantation with a reasonable expectation of success for improving cell transplantation into the recipient damaged tissues, thus, producing improved and/or functional tissue "comprising muscle cells" within the broadest meaning of the instant claims as suggested by Kocher et al. and Kalka et al. and as taught by US 5,199,942 (Gillis). One of skill in the art would have been motivated to *ex vivo* expand the stem or progenitor cells prior transplantation for the expected benefits in expanding or increasing number of harvested cells as taught by Kalka et al. and taught by US 5,199,942 (Gillis). One of skill in the art would have been motivated to use cells derived from a donor that is HLA-matched to the recipient for the expected benefits in minimizing immune response and avoiding transplant rejection (US 7,097,833).

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary. The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

2. Claims 1, 9-14, 17, 18, 20, 21, 24-31, 35, 39-47 as amended and new claims 48 and 49 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,387,369 (Pittenger et al) and US 6,261,549 (Fernandez et al) taken with Orlic et al. (IDS reference; Nature. 2001, Vol. 410, pages 701-705) and Orlic et al. ("Cytokine-mobilized stem cells traffic to infracted hearts and regenerate functional myocardium resulting in improved survival". Blood. 2001. Vol. 98, No. 11, part 1, page 810a.).

Claims are directed to a method of producing a graft of muscle tissue in damaged or diseased tissue of a human in need thereof, comprising steps of (a) administering a mobilization factor to a donor to mobilize stem cells into peripheral blood, the donor being HLA-matched to a recipient; (b) isolating stem cells from peripheral blood of the donor by apheresis; and (b) implanting a population of the isolated stem cells into the tissue of recipient; whereby implantation produces a graft of muscle tissue in the damaged or diseased tissue. Some claims are/are further drawn to the damaged or diseased tissue(s) including tissue striated muscle, ischemic tissue, necrotic tissue, myocardium, skeletal muscle, heart. Some claims are further drawn to administration of engraftment factor to promote engraftment of the stem cells in the subject. Some claims are further drawn to fractionating the stem cells prior implantation including FACS and density gradient centrifugation. Some claims are further drawn to additional

step of ex vivo expanding the cells prior to the implanting step. Some claims are further drawn to implanting the cells at the site of disease or damage. Some claims are further drawn to the use of mesenchymal stem cells in the method for of treating damaged muscle tissue.

US 6,387,369 teaches a method for regeneration of repair of striated cardiac muscle or for producing a graft of muscle tissue by implanting mesenchymal stem cells (MSCs) in the damaged tissue, for example: see entire document including col. 1, lines 41-50. The preferred stem cells are autologous MSC cells (col. 2, line 23), thus, clearly being HLA-matched cells. US 6,387,369 also teaches administration of engraftment factor such as collagen biomatrix together with MSCs (col. 6, lines 64-67) for regeneration of repair of striated cardiac muscle or for producing a graft of muscle tissue

Although the source for the isolation of the MSCs in the method of administration is a generic "MSC-containing tissue" as disclosed by US 6,387,369 (for example: col. 1, line 61.), the other cited patent US 6,261,549 teaches that the MSCs intended for administration and muscle tissue repair are collected from the peripheral blood of the donors treated the mobilization factors including G-CSF and/or GM-CSF, for example: see entire document including abstract. Both cited patents US 6,387,369 and US 6,261,549 also encompass cell sorting and ex-vivo expansion of the cells prior to administration.

Further, the cited references by Orlic et al. teach and demonstrate that bone marrow-derived stem cells mobilized by cytokines into peripheral blood regenerate the infarcted myocardium.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use mesenchymal stem cells mobilized into peripheral blood

for implantation into the damaged striated muscle tissue with a reasonable expectation of success in producing a graft of muscle tissue because the prior art teaches and/or suggests the use of mesenchymal stem cells mobilized by cytokines into peripheral blood for regeneration of striated cardiac muscle as adequately demonstrated by the cited references. The prior art clearly teaches the use of autologous MSC cells, inherently being HLA-matched cells, as preferred source of cell for transplantation. In alternative, one of skill in the art would have been motivated to use cells derived from a donor that is HLA-matched to the recipient for the expected benefits in minimizing immune response and avoiding transplant rejection.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 9/14/2007 have been fully considered but they are not found persuasive.

1. With regard to the claim rejection under 35 U.S.C. 103(a) as being unpatentable over Kocher et al. and Kalka et al. taken with US 5,199,942 (Gillis) applicant argues that the cited references are silent about some limitations encompassed by the claims including the use of engraftment factors, HLA-matching of donor and recipient and production of "muscle cells" (response pages 9-10) and applicants further argue that there is no suggestion/motivation to

combined the cited references with reasonably expectation in success suggest in production of "muscle cells" (response pages 10-11).

These arguments have no persuasive grounds.

The general concept and the sequence of active step as disclosed by the cited prior art (Kocher et al., Kalka et al., US 5,199,942 (Gillis)) is the same as encompassed by the presently claimed method comprising steps of mobilization (recruitment into peripheral blood), isolation and implantation of stem cells in combination with engraftment factors. Moreover, the identical specific factors as presently claimed are also taught by the cited references including IL-1 (US 5,199,942) and Flt-3 ligand (US 6,713,052).

Further, although the particular experimental models in the methods Kocher et al. and Kalka et al involve xenograft implantation of human stem cells into rodent models, one of skill in the art would clearly be motivated to use stem cells from donor who is HLA matched to recipient for the expected benefits in avoiding immune reaction, graft rejections and GVHD complications. Moreover, the prior art clearly teaches and suggests to use cells derived from a donor that is HLA-matched to the recipient in the method of improving function of damaged muscle or heart (US 7,097,833).

With regard to argument as drawn to development or production of "muscle cells", it is noted that the claimed term "a graft comprising muscle cells in the damaged or diseased tissue" is rather vague and broad as claimed and as disclosed. First, the formation of muscle cells from the stem cells as argued by applicant is not required by the instant claims because "a graft comprising muscle cells" comprises also some other cells. Second, no histological analysis of a newly formed "graft comprising muscle cells" from the implanted stem cells including

hematopoietic cells is disclosed by the applicant (specification pages 24-26) in order to clearly define the intended effects as argued. Thus, given a broadest reasonable interpretation to the claimed invention in light of specification, the generic claimed limitation such as "producing a graft comprising muscle cells" as a whole muscle tissue also encompasses producing new vascular structures from stem cells in the damaged muscle tissue as a whole comprising muscle cells and vascular structures with endothelial cells. The revascularization protects muscle cells against apoptosis and provides for regeneration and improvement of muscle tissue function as a whole. The cited reference by Kalka et al. teaches that transplantation of human peripheral blood derived stem cells or endothelial progenitors resulted in improved recovery and capillary density in the skeletal muscle tissue of the ischemic hindlimbs (page 3425, last par.), thereby, providing for the muscle tissue salvage (page 3426, col. 1). Thus, the cited references are in the same field of endeavor and seek to solve the same problems as the instant application and claims. Moreover, endothelial progenitor cells are inherent progenitors of heart muscle cells in view of the applicant's IDS reference by Strauer et al. (page 930, col.1, last par.).

With regard to the use of mobilization and engraftment factors applicant's argument are not found particularly persuasive because the prior art clearly teaches and suggest the use of both mobilization factors for isolation of stem cells and engraftment factors in combination with stem cell for implantation and engraftment of stem cells. Moreover, the same particular mobilization and engraftment factors are clearly disclosed by the cited references. For example: US 5,199,942 (Gillis) teaches administration of mobilization (recruitment) factors prior to harvest of stem cells from peripheral blood and administration of engraftment factors subsequent to implantation of the stem cells (col. 3, lines 29-45) including IL-1 as well as GM-CSF, IL-3, SCF, etc. US

6,713,052 teaches the use of Flt-3 as a mobilization factor similar to G-CSF and GM-CSF. Thus, the cited prior art demonstrates that various mobilization and engraftment factors can be used as equivalents for mobilization and engraftment of stem cells. Therefore, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary. The instant specification lacks evidence about formation of muscle cells from engrafted stem cells that were collected and implanted with the help of mobilization and engraftment factors. The instant specification even lacks evidence about engraftment of stem cells that were collected and implanted with the help of mobilization and engraftment factors.

Thus, applicant's arguments as drawn to formation of muscle cells from stem cells with the help of either generic or specific mobilization and engraftment factors have no persuasive grounds because neither claims clearly require formation of muscle cells from engrafted stem cells nor objective evidence based on the instant specification disclosure supports this argument.

2. With regard to the claim rejection under 35 U.S.C. 103(a) as being unpatentable over US 6,387,369 (Pittenger et al) and US 6,261,549 (Fernandez et al) taken with Orlic et al. (Nature. 2001, Vol. 410, pages 701-705) and Orlic et al. (Blood. 2001. Vol. 98, No. 11, part 1, page 810a) applicant's main argument is that the cited references are silent about HLA-status of donor of stem cells. However, the stem cells that are used for muscle repair in the method of US 6,387,369 (Pittenger et al) are mesenchymal stem cells. It is well known that mesenchymal stem cells are immunologically neutral cells, they are invisible for immune system and they do not express immunologically relevant cell surface markers. Therefore, MSCs need not to be MHC (or HLA) matched as evidenced by US 6,355,239, for example: see col. 1, lines 20-50. Thus, the

prior art references cited in the office action are silent about HLA status of donor stem cells since the use of mesenchymal stem cells does need matching of donors accordingly HLA status.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1657

November 21, 2007

VERA AFREMOVA

PRIMARY EXAMINER